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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/466,035

12/17/1999

MATTI SALLBERG

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9697

27476

7590

05/08/2009

NOVARTIS VACCINES AND DIAGNOSTICS INC.  
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EXAMINER

WEHBE, ANNE MARIE SABRINA

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

05/08/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/466,035	<b>Applicant(s)</b> SALLBERG ET AL.	
	<b>Examiner</b> Anne Marie S. Wehbe	<b>Art Unit</b> 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5, 12, 13 and 26-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 12, 13 and 26-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/3/09</u> .  | 6) <input type="checkbox"/> Other: _____                          |

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**DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/3/09 has been entered. Applicant's response and Declaration under 37 CFR 1.132 by William B. Klimstra also filed on 3/3/09 have been entered. No claims have been amended, added, or canceled. Claims 1-5, 12-13, and 26-29 remain pending and under examination in the instant application. An action on the merits follows.

It is noted that those sections of Title 35, US code not included in this action can be found in the previous office action.

***Information Disclosure Statement***

Applicant's IDS filed on 3/3/09 has been considered by the examiner. An initialed copy is attached to this office action.

***Claim Rejections - 35 USC § 103***

The rejection of claims 1-5, 12-13, and 26-29 under 35 U.S.C. 103(a) as being unpatentable over WO 95/07994 (1995), hereafter referred to as Dubensky et al., in view of Hu

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et al. (1991) AIDS Res. Hum. Retrovir., Vol. 7 (7), 615-620 is maintained. Applicant's arguments and the Declaration under 37 CFR 1.132 by William B. Klimstra have been fully considered but have not been found persuasive in overcoming the instant rejection for reasons of record as discussed in detail below.

The applicant reiterates their previous argument that since Hu et al. teaches the use of a prime boost strategy with a replicating vaccinia virus vector, the skilled artisan would not be motivated to combine the teachings of Hu et al. with those of Dubensky et al. who teaches the use of non-replicating vectors, i.e. alphavirus vectors or layered eukaryotic systems. More specifically, the applicant now argues that the Declaration by Dr. Klimstra states that since vaccinia virus is a DNA virus and the alphavirus is an RNA virus, immunization with each results in different kinds of immune responses such that there would have been no reasonable expectation of success in using the prime-boost strategy developed with vaccinia virus for alphavirus vectors or layered eukaryotic vectors.

In response, it is first noted that the claims as written do not require any particular type of immune response to be generated. The claims under examination simply recite that the method results in the generation of an immune response against the encoded intracellular pathogen antigen. Second, with the exception of claim 12, the claims are not limited to the use of alphavirus vectors. In fact, the independent claims and dependent claims 1-5, 13, 26 and 28-29 are not even limited to RNA viruses as parvoviruses are DNA viruses and layered eukaryotic vector initiation systems comprise a second layer which can include DNA viruses such as poxviruses. As such, applicant's arguments regarding RNA versus DNA viruses are only

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applicable to claims 12 and 27 and are not found persuasive in regards to claims 1-5, 13, 26 and 28-29 which encompass DNA viruses.

In regards to claims 12 and 27, the Declaration under 37 CFR 1.132 by William B. Klimstra, has been fully and respectfully considered. It is noted for the record that William B. Klimstra is not a named inventor in this application. Dr. Klimstra states that DNA viruses and RNA viruses stimulate different types of immune responses, and refers to two post-filing publication as evidence that the tropism of vaccinia virus is different than that of alphavirus. In view of these differences, Dr. Klimstra concludes that the skilled artisan would not have expected success extrapolating from the results of Hu's DNA-based Vaccinia virus prime/boost approach to an RNA-based alphavirus prime/boost approach. In response, it is first noted that both the cited Yu et al. and Sanchez-Puig et al. references were published 10 and 8 years respectively after the effective filing date of the instant application, which is September 17, 2006, and thus clearly do not reflect what was known by the skilled artisan at the time of filing. In addition, while Dr. Klimstra states that alphaviruses exhibit tropism for macrophages and dendritic cells while vaccinia virus has tropism for monocytes, the post-filing evidence is silent as to the tropism of alphaviruses and in fact teaches that vaccinia virus infects not only monocytes, but macrophages and both immature and mature dendritic cells as well (see Yu et al.). Further, while the opinion of Dr. Klimstra that the skilled artisan would not have found a reasonably expectation of success in boosting alphavirus with protein based on the Hu et al. experiments with vaccinia virus because of differences in immune stimulation between vaccinia virus and alphavirus has been respectfully considered, no actual evidence has been provided that the result of immunization with vaccinia virus results in any meaningful difference in qualitative

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or quantitative immune responses generated against any specific antigen. It is also noted that claim 27 is not limited to alphavirus vectors and the Declaration is silent as to the tropism or differences between poxviruses and retroviruses.

Further, as noted above, the claims are not limited to the generation of any particular type of immune response. Dubensky et al., as set forth in the rejection of record, teaches the use of recombinant alphavirus and eukaryotic layered vector initiation systems, which comprise retroviruses and adeno-associated viruses vectors, encoding immunogenic antigens derived from pathogens including HIV and hepatitis to stimulate antigen specific immune responses including both antibody and cell mediated immune responses. The Hu et al. reference clearly demonstrates that both a prime/boost strategy using the same vaccinia vector and a prime/boost strategy using the vector followed by a protein result in the generation of antigen specific antibodies. Thus, regardless of any alleged differences between RNA and DNA viruses, Dubensky et al. and Hu et al. teaches that both are capable of inducing antigen specific antibodies following immunization.

Further, as discussed in detail in previous office actions, Hu et al. also provides motivation to use a prime/boost strategy where a vector immunization is followed by a protein immunization by demonstrating that this combination results in neutralizing titers of antibody. Therefore, it is maintained that since Dubensky et al. teaches that both replicating and non-replicating alphaviruses and layered eukaryotic vector initiation systems can induce antigen specific immune responses and further teaches a "prime and boost" protocol using multiple vector administrations, and since Hu et al. teaches that boosting with protein is more effective than boosting with vector, it would have been *prima facie* obvious to the skilled artisan at the time of filing to utilize the prime boost approach taught by Hu et al. in the immunization

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methods of Dubensky et al. Further, based on the state of the art in generating immune responses using DNA and RNA viruses at the time of filing as evidenced by Dubensky et al. and Hu et al., and the breadth of the claims, it is maintained that one of skill in the art at the time of filing would have had a reasonable expectation of success in generating an immune response by administering a replication incompetent vector, including an RNA based alphaviral vector, encoding a viral antigen followed or preceded by administration of the viral antigen itself.

Therefore, for the reasons set forth above, applicant's arguments and the Declaration by Dr. Klimstra have not been found persuasive in overcoming the rejection of record.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

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Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

*/Anne Marie S. Wehbé/*

Primary Examiner, A.U. 1633